REMARKS

Claims 1-11 were pending in the subject application. Applicant's traversal of the Restriction Requirement was found to be persuasive, and Groups II-III were joined with elected Group I. Claims 1-11 are pending and examined.

In view of the remarks that follow, Applicant respectfully requests reconsideration of the outstanding rejection to the claims.

The Rejection of Claims Under 35 U.S.C. §103(a)

In paragraph 4, the Examiner rejected claims 1-11 under 35 U.S.C. §103(a) as allegedly unpatentable over Nguyen et al., (1997), in view of Relf et al., (1997), Li et al., (1994), Cheales-Siebenaler et al., (1999) and Petrakis (1993)).

The Office asserts that the teachings of Nguyen and Li made it obvious at the time of the invention to "diagnose and determine the progress of breast cancer," and to "measure bFGF in nipple breast fluid," because "Petrakis teach that nipple fluid contains several types of exfoliated breast cells and Relf teach the detection of increased levels of bFGF in breast tumor tissue as compared to normal breast tissue." (Office Action, page 3).

The Legal Standards for Establishing Obviousness Under 35 U.S.C. §103

As stated in MPEP §2142, three (3) criteria must be met to establish a *prima facie* case of obviousness:

> First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference must

> teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based upon applicants' disclosure.[1]

The teaching or suggestion to make the claimed combination, and the reasonable expectation of success, must both be found in the prior art, not in the Applicant's disclosure (In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)).

Obviousness is a question of law based on findings of underlying facts relating to the prior art, the skill of the artisan, and objective considerations. See Graham v. John Deere Co., 383 U.S. 1, 17, 148 USPQ 459, 467 (1966). To establish a prima facie case of obviousness based on a combination of the content of various references, there must be some teaching, suggestion or motivation in the prior art to make the specific combination that was made by the applicant. In re Raynes, 7 F.3d 1037, 1039, 28 USPQ2d 1630, 1631 (Fed. Cir. 1993); In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992).

Obviousness cannot be established by hindsight combination to produce the claimed invention. In re Gorman, 933 F.2d 982, 986, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991). As discussed in Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1143, 227 USPQ 543, 551 (Fed. Cir. 1985), it is the prior art itself, and not the applicant's achievement, that must establish the obviousness of the combination.

The teachings of the references, their relatedness to the field of the applicant's endeavor, and the knowledge of persons of ordinary skill in the field of the invention, are all relevant considerations. See In re Oetiker, 977 F.2d at 1447, 24 USPQ2d at 1445-46; In re Gorman, 933 F.2d at 986-87, 18 USPQ2d at 1888; In re Young, 927 F.2d 588, 591, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991). When the references are in the same field as that of the applicant's invention, knowledge thereof is presumed. However, the test of whether it

[1] MPEP §2142, *citing In re Vaeck*, 957 F . 2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

would have been obvious to select specific teachings and combine them, as did the applicant, must still be met by identification of some suggestion, teaching, or motivation in the prior art, arising from what the prior art would have taught a person of ordinary skill in the field of the invention. In re Fine, 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988).

The Patent Office Has Not Established A *Prima Facie* Case Of Obviousness

The claimed invention is directed to a method for diagnosing breast cancer, or a high risk of breast cancer, by measuring basic fibroblast growth factor (bFGF) in a test sample of nipple fluid, and comparing the level of bFGF in the test sample with samples from subjects not having breast cancer.

The Patent Office has not established a *prima facie* case of obviousness in connection with the claimed invention. The cited references do not teach or suggest the detection of bFGF in nipple breast fluid, or correlation of bFGF levels with the presence or absence of breast cancer, as disclosed and demonstrated in the instant application.

As stated by the Office, the Nguyen articles disclose variations in bFGF levels in urine and serum of patients with breast tumors. Nguyen et al. do not describe or suggest measuring bFGF in nipple fluid, or that levels of bFGF in nipple fluid correlate with the presence or absence of breast cancer as claimed in this application.

Relf et al. describe detection of bFGF in tumor tissues, not bodily fluids.

Li et al. describe detection of bFGF in the CSF of patients with brain tumors.

Petrakis et al. teach the presence of exfoliated breast cells in nipple aspirate fluid.

None of the cited references provide the suggestion or motivation to test nipple fluid for bFGF levels. The articles do not describe or suggest measuring bFGF in nipple fluid, or that levels of bFGF in nipple fluid correlate with the presence or absence of breast cancer as claimed in this application.

Moreover, as pointed out by Dr. Nguyen, the inventor of the present application, in her 1997 review article, there is overlap in bFGF measurements in sera and urine such that bFGF values in these fluids cannot provide an accurate diagnostic assay for breast cancer using these fluids. ("Based on the results from the above studies involving different types of tumor, it appears that the measurement of angiogenic growth factors is not specific enough for screening or diagnosis of cancer." (Nguyen, 1997, page 34, second column).

Absent a specific teaching that bFGF levels in nipple fluids correlate with the presence or absence of breast tumors, there would have been no reasonable expectation of success for the presently claimed method, particularly in view of Dr. Nguyen's 1997 review suggesting the lack of specificity of bFGF levels in serum and urine, for diagnosis of cancer. The fact that nipple fluid contains exfoliated breast cells as taught by Petrakis does not suggest that the fluid will contain bFGF, or that the levels of bFGF if present in the nipple fluid, will correlate with the presence or absence of breast cancer.

Therefore, the Office has not established or supported a prima facie case for obviousness of the presently claimed invention.

CONCLUSION

In view of the Applicant's remarks, Applicant contends that the claims of the subject application, are in condition for allowance. Accordingly, Applicant requests issuance of a notice of allowance.

No fee is deemed necessary in connection with the filing of this response. If, however, a fee is deemed necessary, the Patent Office is authorized to charge the amount of such fee to Deposit Account No. 50-0306.

Respectfully submitted,

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